Research Article

The Impact of Exercise on DNA Damage in Athletes: Causes, Mechanisms, and Case Studies

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Abstract.
Although physical activity is important for the athlete's health and performance, it may also lead to Deoxyribonucleic Acid (DNA) damage, which may have long-term health consequences and affect performance. This article summarizes different types of DNA damage that may occur in athletes, including their potential risk causes, such as mechanical stress, heat stress, and oxidative stress. Furthermore, several mechanisms by which physical activity might lead to DNA damage and affect health and performance are also discussed. Various strategies such as diet and nutrition, antioxidant supplements, cooling strategies, and recovery modalities are also presented to mitigate, prevent, and minimize the potential DNA damage upon physical activities. This article also highlights case studies of athletes who have experienced DNA damage and the effects on their performance and health. In summary, this article offers valuable perspectives on the intricate relationship between physical activity and DNA damage as well as the importance of addressing this issue in the context of athletic performance and health.

Keywords: athlete, DNA damage, exercise, RONS

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1. Introduction

Exercise has been widely known for its beneficial effects for human health and wellness [1]. However, evidences show some opposite effects of exercise associated with DNA damage. This occurs mainly due to the production of reactive oxygen and nitrogen species (RONS) in exercises. Overproduction of RONS exceeds antioxidant production in neutralizing the effects of RONS that can result in DNA damage. As vulnerable target of RONS, DNA damage may cause genetic instability if happens continuously [2,3].

RONS are generated in skeletal muscles mainly through mitochondrial electron transport chain during cellular respiration [4]. As reactive oxygen and nitrogen species (RONS) gather within the cell, whether generated through metabolic signaling pathways such as NADPH or originating from external sources, they are counteracted by scavenging

antioxidant mechanisms. Reactive oxygen and nitrogen species (RONS) play significant roles in controlling fundamental processes like cellular growth, differentiation, and apoptosis [2,5,6].

However, accumulation of RONS also has negative impact in human body, especially in athletes. Studies reported the incidence of sudden cardiac death (SCD) in young athlete are most commonly caused by left ventricular hypertrophy (LVH) which are clinically indistinguishable from physiological LVH in response to exercise and probably related to DNA damage [7]. Other study showed some cases of DNA repair deficiency and senescence in contact sports athletes with history of mild traumatic brain injury (mTBI) [8]. Study conducted with comet assay also suggested that endurance exercise results in DNA damage [9]. Based on the previous background, the objective of this study was to examine and evaluate the collective impact of research studies which discusses DNA damage resulting from various forms of exercise.

2. Methods

The method we use in this study is a study literature from reliable scientific references in search engines such as Web of Science, PubMed, MEDLINE, EMBASE, and Scopus in last ten years up to 2022.

3. Results and Discussion

Some studies find that physical activities could lead to DNA damage, but some also suggest otherwise. Study by Laomax suggest that chlorine exposure and chronic endurance training reduce Club cell protein 16 (CC16) levels and the ratio of CC16 to surfactant-associated protein D. that leads to lung growth restriction and this study was carried out to swimmer athletes. They also suggest that retirement will help to partially reverse this condition in children and adolescence athletes [10]. Study by Arent, 2010 and Carrera-Quintanar, 2022 show the occurrence of oxidative stress through increase of MDA level and creatine kinase in football player [11][12].

In contrast, several studies show protective effect of exercise such as regular physical activity protective effect against DNA damage in lymphocytes by increase in antioxidant capacity [13]. Neubauer also proposes that oxidative DNA damage may have been offset by the antioxidant responses triggered by training and exercise [14]. Liang, 2022 also noted that treadmill exercise decreases Bcl-2 and Bax values in the body, enhances

mitochondrial DNA integrity and increases telomerase activity in myocardial cells [15]. Study by Tryfidou, 2019 described that in acute aerobic exercise, there is a notable rise in DNA damage right after engaging in short-term aerobic exercise, and this elevation remains notable between 2 hours and 24 hours afterward, but not within the period of 5 to 28 days following the exercise session [2]. The opposite effect of various exercise related to DNA damage describes in detailed in Table 1.

The most important thing is that Short-term exercise leads to a temporary rise in RONS production as a result of heightened activity in mitochondria and other metabolic pathways. This may subsequently induce oxidative stress and DNA damage. The extent of ROS increase is influenced by exercise factors such as intensity, duration, and frequency. Numerous studies also propose that the connection between exercise and DNA damage might be elucidated by the hormesis theory, which is somewhat simplistic and therefore constrained [2][16]. Top of Form

The hormesis theory explains how exercise regulates both beneficial and detrimental effects mediated by RONS, by amplifying DNA oxidation between two poles: physical inactivity and overtraining. It is noteworthy that consistent exercise has been demonstrated to boost the body's antioxidant defense mechanisms and promote DNA repair mechanisms. Conversely, excessively intense activity levels may result in DNA damage, leading to the suggestion that the interplay among exercise, ROS, and DNA damage could adhere to the curve depicted in Figure 1 [2][16].

Nevertheless, the precise threshold between the advantageous outcomes of consistent exercise and the onset of overtraining, which is linked to heightened oxidative damage and inadequate DNA repair, remains uncertain. Taking this into account, engaging in regular exercise, especially aerobic exercise, is likely to mitigate DNA damage owing to elevated antioxidant capacity and enhanced DNA repair capabilities [2][16].

4. Conclusion

In summary, the relationship between exercise and DNA damage could potentially be elucidated by the hormesis theory where the dose of exercise, training intensity and frequency, plays significant roles to the outcomes. The hormesis theory outlines how exercise influences both beneficial and detrimental effects of RONS activity, by enhancing DNA oxidation which results in DNA damage.

Table 1: Opposite effects of various exercise related to DNA damage.

Types of DNA Damage	Exercise / Sport	Long-term Effect	Prevention	References
Reduction in levels of Club cell protein 16 (CC16) and the ratio of CC16 to surfactant-associated protein D. Top of Form Bottom of Form	Swimming: chlorine exposure and chronic endurance training	lung growth restriction	partially reversible in early retirement	Lomax, 2016 [10]
Oxidative stress	Football: increase MDA level	-	polyphenolic antioxidant and anti-inflammatory supplements	Carrera-Quintanar, 2022 [12]
Oxidative stress	Football: increase creatine kinase and oxidative stress biomarker	-	antioxidant and nutraceutical blend supplements	Arent, 2010 [11]
Oxidative stress by increasing ROS and creatine kinase (CK) level	Athletic sprint	-	strength training should be combined with proper recovery in between each session	Affonso, 2019 [17]
Protective effect against DNA damage in lymphocytes by increase in antioxidant capacity	Regular physical activity	-	-	Soares, 2015 [13]
The oxidative damage to DNA may have been offset by the antioxidant responses triggered by training and exercise.	Regular physical activity	-	-	Neubauer, 2019 [14]
Decrease the levels of Bcl-2 and Bax in the body, enhance mitochondrial DNA integrity, and increase telomerase activity in myocardial cells.	Treadmill exercise	slow down the aging process	-	Liang, 2022 [15]
A notable elevation in DNA damage after a short-term aerobic exercise that persists significantly between 2 hours and 1 day afterward.	Aerobic exercise	-	-	Tryfidou, 2020 [2]
Reduction of DNA repair proteins levels in mild traumatic brain injury (mTBI) or concussion brains resulting in DNA damage and cellular senescence that lead to neurobehavioral and/or psychiatric symptoms or cognitive dysfunction and/or dementia.	Contact sports: football, hockey, rugby, and boxing.			Schwab, 2019 [8]

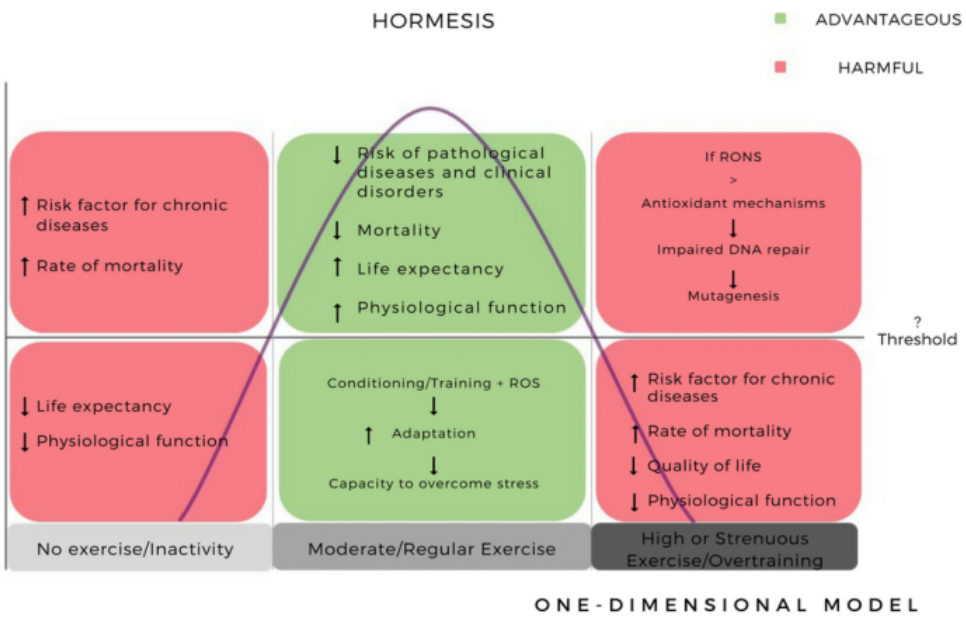

Figure 1: Hormesis theory in different intensity of exercises [2].

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